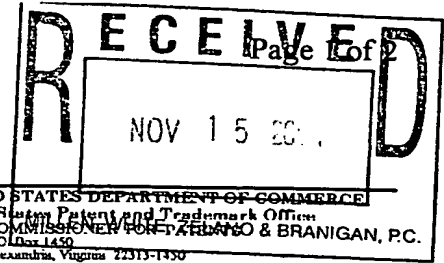**UNITED STATES PATENT AND TRADEMARK OFFICE**

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... & BRANIGAN, P.C.

U.S. APPLICATION NUMBER NO.	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
09/868,098	Beate Diefenbach	MERCK 2251

INTERNATIONAL APPLICATION NO.
PCT/EP99/09842

I.A. FILING DATE	PRIORITY DATE
12/11/1999	

23599
MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
2200 CLARENDON BLVD.
SUITE 1400
ARLINGTON, VA 22201

CASE _____ Response Due
ACTION _____
DUE DATE _12/12/04_

CONFIRMATION NO. 5446
371 FORMALITIES LETTER

OC00000014338055

Date Mailed: 11/12/2004

NOTIFICATION OF DEFECTIVE RESPONSE

The following items have been submitted by the applicant or the IB to the United States Patent and Trademark Office as a Designated / Elected Office (37 CFR 1.495)

- Original Specification filed on 06/14/2001
- Claims filed on 06/14/2001
- Oath or Declaration filed on 06/14/2001
- Initial Application Filing Fees filed on 06/14/2001
- Copy of the International Application filed on 06/14/2001
- Copy of the International Search Report filed on 06/14/2001
- Copy of IPE Report filed on 10/23/2003
- Preliminary Amendments filed on 06/14/2001
- Information Disclosure Statements filed on 08/15/2001
- Biochemical Sequence Diskette filed on 08/24/2004
- Oath or Declaration filed on 06/14/2001
- Biochemical Sequence Listing filed on 08/24/2004
- Copy of references cited in ISR filed on 06/14/2001
- U.S. Basic National Fees filed on 06/14/2001

CASE _____
ACTION _____
DUE DATE _____

Applicant's response filed 08/24/2004 is hereby acknowledged. The following requirements set forth in the NOTIFICATION of MISSING REQUIREMENTS mailed 09/08/2003 have not been completed.

Applicant is required to complete the response within a time limit of ONE MONTH from the date of this Notification or within the time remaining in the response set forth in the Notification of Missing Requirements, whichever is the longer. No extension of this time limit may be granted under 37 CFR 1.136, but the period for response set in the Notification of Missing Requirements may be extended under 37 CFR 1.136(a).

The following items MUST be furnished within the period set forth below:

- The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 CFR 1.821-1.825 for the following reason(s):

- The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A substitute computer readable form must be submitted as required by 37 CFR 1.825(d).
- APPLICANT MUST PROVIDE:
  - An initial or substitute computer readable form (CRF) of the "Sequence Listing."

- For questions regarding compliance to 37 CFR 1.821-1.825 requirements, please contact:
  - For Rules Interpretation, call (703) 308-4216
  - To Purchase PatentIn Software, call (703) 306-2600
  - For PatentIn Software Program Help, call (703) 306-4119 or e-mail at patin21help@uspto.gov or patin3help@uspto.gov

Applicant is reminded that any communications to the United States Patent and Trademark Office must be mailed to the address given in the heading and include the U.S. application no. shown above (37 CFR 1.5)

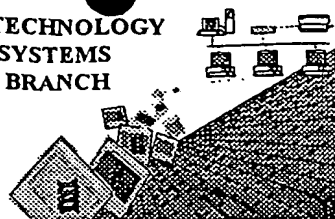*A copy of this notice MUST be returned with the response.*

MAMIE P PERSON

Telephone: (703) 305-3737

PART 1 - ATTORNEY/APPLICANT COPY

U.S. APPLICATION NUMBER NO.	INTERNATIONAL APPLICATION NO.	ATTY. DOCKET NO.
09/868,098	PCT/EP99/09842	MERCK 2251

FORM PCT/DO/EO/916 (371 Formalities Notice)

RAW SEQUENCE LISTING
ERROR REPORT

The Biotechnology Systems Branch of the Scientific and Technical Information
Center (STIC) detected errors when processing the following computer readable
form:

Application Serial Number: _09/868,098A_

Source: _Pu7/o9_

Date Processed by STIC: _10/24/04_

THE ATTACHED PRINTOUT EXPLAINS DETECTED ERRORS.
PLEASE FORWARD THIS INFORMATION TO THE APPLICANT BY EITHER:
1) INCLUDING A COPY OF THIS PRINTOUT IN YOUR NEXT COMMUNICATION TO THE
APPLICANT, WITH A NOTICE TO COMPLY or,
2) TELEPHONING APPLICANT AND FAXING A COPY OF THIS PRINTOUT, WITH A
NOTICE TO COMPLY
FOR CRF SUBMISSION AND PATENTIN SOFTWARE QUESTIONS, PLEASE CONTACT
MARK SPENCER, TELEPHONE: 571-272-2510; FAX: 571-273-0221

TO REDUCE ERRORED SEQUENCE LISTINGS, PLEASE USE THE <u>CHECKER
VERSION 4.2 PROGRAM</u>, ACCESSIBLE THROUGH THE U.S. PATENT AND
TRADEMARK OFFICE WEBSITE. SEE BELOW FOR ADDRESS:
http://www.uspto.gov/web/offices/pac/checker/chkrnote.htm

Applicants submitting genetic sequence information electronically on diskette or CD-Rom should be aware that there is
a possibility that the disk/CD-Rom may have been affected by treatment given to all incoming mail.
Please consider using alternate methods of submission for the disk/CD-Rom or replacement disk/CD-Rom.
<u>Any reply including a sequence listing in electronic form should NOT be sent to the 20231 zip code address for the
United States Patent and Trademark Office, and instead should be sent via the following to the indicated addresses:</u>

1. EFS-Bio (**<http://www.uspto.gov/ebc/efs/downloads/documents.htm>** , EFS Submission
User Manual - ePAVE)
2. U.S. Postal Service: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450
3. Hand Carry, Federal Express, United Parcel Service, or other delivery service (EFFECTIVE 06/05/04):
U.S. Patent and Trademark Office, 220 20th Street S., Customer Window, Mail Stop Sequence, Crystal Plaza Two, Lobby,
Room 1B03, Arlington, VA 22202

Revised 05/17/04

Raw Sequence Listing Error Summary

ERROR DETECTED	SUGGESTED CORRECTION	SERIAL NUMBER: 09/868,098A

ATTN: NEW RULES CASES: PLEASE DISREGARD ENGLISH "ALPHA" HEADERS, WHICH WERE INSERTED BY PTO SOFTWARE

1 _____ Wrapped Nucleics
Wrapped Aminos

The number/text at the end of each line "wrapped" down to the next line. This may occur if your file was retrieved in a word processor after creating it. Please adjust your right margin to .3; this will prevent "wrapping."

·2 _____ Invalid Line Length The rules require that a line not exceed 72 characters in length. This includes white spaces.

3 _____ Misaligned Amino
Numbering

The numbering under each 5th amino acid is misaligned. Do not use tab codes between numbers; use space characters, instead.

4 _____ Non-ASCII

The submitted file was not saved in ASCII(DOS) text, as required by the Sequence Rules. Please ensure your subsequent submission is saved in ASCII text.

5 _____ Variable Length

Sequence(s) _____ contain n's or Xaa's representing more than one residue. **Per Sequence Rules, each n or Xaa can only represent a single residue. Please present the maximum number of each residue having variable length and indicate in the <220>-<223> section that some may be missing.**

6 _____ PatentIn 2.0
"bug"

A "bug" in PatentIn version 2.0 has caused the <220>-<223> section to be missing from amino acid sequences(s) _____. Normally, PatentIn would automatically generate this section from the previously coded nucleic acid sequence. Please manually copy the relevant <220>-<223> section to the subsequent amino acid sequence. **This applies to the mandatory <220>-<223> sections for Artificial or Unknown sequences.**

7 _____ Skipped Sequences
(OLD RULES)

Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence:
(2) INFORMATION FOR SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
(i)   SEQUENCE CHARACTERISTICS: (Do not insert any subheadings under this heading)
(xi) SEQUENCE DESCRIPTION:SEQ ID NO:X: (insert SEQ ID NO where "X" is shown)
This sequence is intentionally skipped

Please also adjust the "(ii) NUMBER OF SEQUENCES:" response to include the skipped sequences.

8 _____ Skipped Sequences
(NEW RULES)

Sequence(s) _____ missing. If intentional, please insert the following lines for each skipped sequence.
<210> sequence id number
<400> sequence id number
000

9 _____ Use of n's or Xaa's
(NEW RULES)

Use of n's and/or Xaa's have been detected in the Sequence Listing.
Per 1.823 of Sequence Rules, use of <220>-<223> is MANDATORY if n's or Xaa's are present.
In <220> to <223> section, please explain location of n or Xaa, and which residue n or Xaa represents.

10 _____ Invalid <213>
Response

Per 1.823 of Sequence Rules, the only valid <213> responses are: Unknown, Artificial Sequence, or scientific name (Genus/species). <220>-<223> section is required when <213> response is Unknown or is Artificial Sequence

11 _____ Use of <220>

Sequence(s) _____ missing the <220> "Feature" and associated numeric identifiers and responses. Use of <220> to <223> is MANDATORY if <213> "Organism" response is "Artificial Sequence" or "Unknown." Please explain source of genetic material in <220> to <223> section.
(See "Federal Register," 06/01/1998, Vol. 63, No. 104, pp. 29631-32)   (Sec. 1.823 of Sequence Rules)

12 _____ PatentIn 2.0
"bug"

Please do not use "Copy to Disk" function of PatentIn version 2.0. This causes a corrupted file, resulting in missing mandatory numeric identifiers and responses (as indicated on raw sequence listing). Instead, please use "File Manager" or any other manual means to copy file to floppy disk.

13 _____ Misuse of n/Xaa

"n" can only represent a single <u>nucleotide</u>; "Xaa" can only represent a single <u>amino acid</u>

AMC – Biotechnology Systems Branch – 09/09/2003

PCT

RAW SEQUENCE LISTING
PATENT APPLICATION: US/09/868,098A

DATE: 10/24/2004
TIME: 09:37:11

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Output Set: N:\CRF4\10242004\I868098A.raw

see item 4 on Error Summary Sheet

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 3 <110> APPLICANT: Merck Patent GmbH
 5 <120> TITLE OF INVENTION: Inhibitors of Integrins avbeta6
 7 <130> FILE REFERENCE: P9858857-bzrs
 9 <140> CURRENT APPLICATION NUMBER: US/09/868,098A
10 <141> CURRENT FILING DATE: 2001-06-14
12 <160> NUMBER OF SEQ ID NOS: 21
14 <170> SOFTWARE: PatentIn Ver. 2.1
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ERRORED SEQUENCES

mandatory numeric identifier and response needed. If Artificial sequence, or Unknown, use.

Does Not Comply Corrected Diskette Needed

what is "oder"? <2207-<2237 for explanation

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342 <210> SEQ ID NO: 21
343 <211> LENGTH: 10
344 <212> TYPE: PRT                    <213>
346 <220> FEATURE:
347 <221> NAME/KEY: SITE
348 <222> LOCATION: (1)
349 <223> OTHER INFORMATION: Xaa = each natural aa, and Nle, homo-Phe,
350       Phg oder H, N-terminal: H oder Acetyl
352 <220> FEATURE:
353 <221> NAME/KEY: SITE
354 <222> LOCATION: (3)
355 <223> OTHER INFORMATION: Xaa = each natural aa, and hom- Phe, Phg,
356       Nle
358 <220> FEATURE:
359 <221> NAME/KEY: SITE
360 <222> LOCATION: (6)..(7)
361 <223> OTHER INFORMATION: Xaa= each natural aa, and Nle, homo-Phe, Phg
363 <220> FEATURE:
364 <221> NAME/KEY: SITE
365 <222> LOCATION: (9)..(10)
366 <223> OTHER INFORMATION: Xaa = each natural aa, and Nle, Phg,
367       homo-Phe; at position 9 also H; C-terminal: OH,
368       NH2, OR, NH-Alkyl, N-Alkyl
370 <213> ORGANISM:
370 <400> SEQUENCE: 21
371 Xaa Arg Xaa Asp Leu Xaa Xaa Leu Xaa Xaa
372  1               5               10
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see p. 2

SEQUENCE LISTING

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<120> Inhibitors of Integrins avbeta6

<130> P9858857-bzrs

<140> PCT/EP99/09842
<141> 1999-12-11

<160> 21

<170> PatentIn Ver. 2.1

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<211> 12
<212> PRT
<213> Artificial Sequence

<220>
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<220>
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 1   5

<210> 3
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<212> PRT
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<220>
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      inhibitory peptide

<400> 3
Arg Thr Asp Leu Asp Ser Leu
 1   5

VERIFICATION SUMMARY
PATENT APPLICATION: US/09/868,098A

DATE: 10/24/2004
TIME: 09:37:12

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Output Set: **N:\CRF4\10242004\I868098A.raw**

.:9 M:270 C: Current Application Number differs, Replaced Current Application Number
.:10 M:271 C: Current Filing Date differs, Replaced Current Filing Date
.:115 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:7 after pos.:0
.:162 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:10 after pos.:0
.:186 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:11 after pos.:0
.:219 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:13 after pos.:0
.:271 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:16 after pos.:0
.:295 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:17 after pos.:0
.:370 M:282 E: Numeric Field Identifier Missing, <213> is required.
.:371 M:341 W: (46) "n" or "Xaa" used, for SEQ ID#:21 after pos.:0